REMARKS

Applicants respectfully requests reconsideration of the present application in view of the foregoing amendments and the following commentary.

I. Status of the Claims

Claims 1-60 were cancelled previously. Claims 86-88 and 123-127 are amended with support in the original specification, for example, at page 15, lines 20-33, the paragraph bridging pages 26 and 27, and at page 67, lines 24-25.

Applicants acknowledge the finality of the outstanding Office Action. Because these amendments (i) are necessitated by the formality objections raised in the final Office Action, (ii) do not require any additional search, and (iii) place the application either in condition for allowance or at least in better condition for appeal, Applicants respectfully request entry of this amendment.

Upon entry, claims 61-127 will be pending, with claims 61-85 and 89-122 withdrawn from examination.

II. Statement of the Substance of the Interview

Applicants thank Examiner Sheridan Swope and Examiner Nashaat Nashed for the courtesies extended during an interview with Applicants' representative, Yang Tang, on May 21, 2008.

During the interview, the objections to the drawings, abstract and the specification were discussed. Examiner Swope clarifies that a SEQ ID NO is required for "EYFP" in the drawings. Since the objections were not raised in the first Office Action, Examiner Swope agreed to consider the necessary amendments in response to the final Office Action upon submission.

In connection with the rejection of claims under 35 U.S.C. §112, first paragraph, for alleged lack of enablement and written description, the Examiners indicated that claims directed to the specific TEV protease and reporter proteins disclosed in the specification would be allowable.

Concerning the rejection of claims under 35 U.S.C. §103(a), the Examiners indicated that further claim amendments and arguments would be considered.

III. Objection to the Drawings

Figures 24 and 25 are objected to for failing to identify a sequence by the SEQ ID NO. Specifically, the Examiner requests that sequence "EYFP" be represented by a SEQ ID NO. Applicants respectfully traverse the grounds of the objection.

In fact, "EYFP" does not represent a polypeptide sequence, as the Examiner contends. Rather, "EYFP" is the abbreviation for "enhanced yellow fluorescent protein" (*see* published application, page 21, paragraph [0380]). As such, no SEQ ID NO is required for figures 24 and 25. Therefore, Applicants respectfully request withdrawal of the objection.

IV. Objection to the Abstract

The abstract is objected to "for being a single, run-on sentence" (final Office Action, page 2, third full paragraph). Applicants respectfully traverse the objection.

Pursuant to MPEP 608.01(b), the language of the abstract should be "clear and concise" and the length of the abstract should not exceed 150 words. There is no requirement of avoiding "a single, run-on sentence" in the abstract however.

In an effort to expedite the prosecution, Applicants submit herewith a rewritten abstract to replace the abstract that the Examiner objects to. Withdrawal of the objection is respectfully requested.

V. Objection to the Specification

The specification is objected to for having two sets of figure legends and for lack of section heading. Applicants respectfully traverse the objection.

As set forth in the foregoing amendments to the specification, the description from page 43, line 26, through page 46, line 15, forms "Brief Description of the Drawings." The description from page 46, line 18, through page 57, line 20, constitutes parts of the "Detailed Description of the Invention." Accordingly, section headings have been added in the specification to conform with the formality requirements.

Applicants respectfully request withdrawal of the objection in view of the amendments.

VI. Rejection of Claims under 35 U.S.C. § 112, second paragraph

Claims 123 and 125-127 are rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. Applicants respectfully traverse the rejection.

Specifically, the Examiner rejected the claims for making reference to specific amino acid residues without identifying the sequence by its SEQ ID NO. The claims have been amended to recite a specific protease, the 27 kDa NIa protease of the Tobacco Etch Virus, and to recite the specific positions of the protease. As described in the specification, the NIa protease is well known in the prior art and the sequence of the NIa protease was disclosed at the time of filing the present application. *See* specification, the paragraph bridging pages 26 and 27.

As evidenced by NCBI Accession No. NP_062908 GI:25013638 (submitted herewith as Exhibit A), the sequence of NIa-Pro protein (from residue 2038 to residue 2279) was disclosed prior to the filing of the present application. The only difference is that the 27 kDa NIa protease of tobacco etch virus has a Gly at the end, i.e., it includes the amino acid at residue 2280.

Otherwise, the sequence is consistent with the 27 kDa NIa protease of tobacoo etch virus, e.g., with His at position 46, Asp at position 81, and Cys at position 151.

Therefore, one skilled in the art would have known the positions of the amino acids recited in the claims. Accordingly, Applicants respectfully request withdrawal of the rejection.

VII. Rejection of Claims under 35 U.S.C. § 112, first paragraph

Claims 86-88 and 123-127 are rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement and written description. Applicants respectfully traverse the rejection.

Specifically, the Examiner contends that the specification does not support any fragments of any TEV protease and any reporter construct cleavable by the TEV protease. Pursuant to the discussions during the Examiners' interview, the claims have been amended to recite the specific TEV protease, the 27 kDa NIa protease of Tobacco Etach Virus, and the specific reporter proteins, which are supported by the specification.

Moreover, the claims do not encompass any fragments of the protease. Rather, the claims relate to fragments that allow reconstitution of a functional protease via interaction of the interaction partners. As described in the specification, each fragment of the protease alone does not have proteolytic activity, and only upon reconstitution, the proteolytic activity is restored. *See* specification, for example, at page 67, lines 24-25. For greater clarity, the claims have been amended to specify that each fragment of the protease alone does not have protease activity.

In view of the foregoing, Applicants respectfully request withdrawal of the rejection.

VIII. Rejection of Claims under 35 U.S.C. § 103(a)

Claims 86-88 remain rejected under 35 U.S.C. § 103(a) for alleged obviousness over Michnick *et al., Methods in Enzymology* 328: 208-230, 2000 ("Michnick"), in view of Bazan *et al., Proc. Natl. Acad. Sci. USA* 85: 7872-7876, 1988 ("Bazan"), and further in view of Carmel *et*

al., FEBS Letters 30: 11-14, 1973 ("Carmel"), as evidenced by Stevens, *Structure* 8: R177-R185, 2000 ("Stevens") and Sawyer *et al., J. Mol. Biol.* 118: 137-208, 1978 ("Sawyer"). Applicants respectfully traverse the rejection.

The teachings of each reference were discussed in the response filed on September 20, 2007. These arguments are incorporated in this response although not explicitly repeated.

In summary, the Examiner's position is that Bazan discloses the homology between the TEV protease and elastase, both of which have twin β-barrel trypsin-like folds. Therefore, one skilled in the art would be motivated to "make and use two fusion proteins, each comprising a single β-barrel structure, for assaying protein/protein interaction" (final Office Action).

First, Applicants submitted in the prior response that one skilled in the art would not have been motivated to substitute elastase for TEV protease and that the rejection is based on hindsight.

Second, even if the skilled person is motivated to combine the teachings of the cited references, one would have been led down the path that each fusion protein for reconstitution should comprise a single β-barrel structure, as the Examiner presumes in the final Office Action. Based on this presumption, the dividing of the protease would have occurred in the hinge region between the β-barrel domains, i.e., between amino acids 90 and 95. *See* Bazan, figures 2a and 3. In contrast, the specification discloses that the regions that are particularly useful for carrying out the method of invention are at a position between amino acids 60 and 80 or at a position between amino acids 95 and 120. Accordingly, the combined teachings of the references would have not led one skilled in the art to the claimed invention.

Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 103(a).

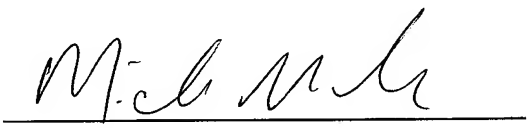
CONCLUSION

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date: July 2, 2008

By 

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5538
Facsimile: (202) 672-5399

Michele M. Simkin
Attorney for Applicant
Registration No. 34,717

NCBI Protein [Sign In] [Regis

PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Book:

Search Protein for Go Clear

Display GenPept Show 5 Send to

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BLink, Conserved Domains, Links

Comment Features Sequence

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